Pat Keady Aerosol Devices Inc.

Project Overview

Aerosol Devices Inc. commercializes a unique aerosol collection technology that mimics the human lung to sample inhalable viruses, and other bioaerosols. This collection method captures all particles down to 0.01 µm in diameter with collection efficiency greater than 90%, covering bare viruses to inhalable bacteria and fungal spores. Competing technologies only collect particles > 0.5 µm in diameter and therefore miss viral particles not associated with droplets or fomites. Our patented, water-based condensation particle growth collection technique is gentle, without imparting mechanical stresses or desiccation upon the bioaerosols, thus maintaining organism viability and cellular integrity upon capture. Our team can provide pre-concentrated, viable, high quality samples that enhance laboratory detection methods, or can be a 'front end" for on-line direct analyses. Our team aims to collaborate in the engineering of a biological detection instrument able to collect, detect and identify harmful bioaerosol activity and to facilitate the determination of a microbe's *in-situ* potential to interact with the environment, or elicit toxic responses.

Teaming Overview and Objectives

The aerosol collection technology project is a partnership between two small businesses, Aerosol Devices Inc. and Aerosol Dynamics Inc. Aerosol Devices, founded in 2014, is an early-age startup with a strong development team including electrical and mechanical engineers, and an analytical chemist. Aerosol Dynamics is a highly-respected 25-year old R&D firm known for its' aerosol measurement innovations. The two companies collaborate closely on the water-condensation growth collector, using technology invented by Aerosol Dynamics that is exclusively licensed to Aerosol Devices for commercialization. Aerosol Devices will take the lead on the future BTO proposal, with contracting options to Aerosol Dynamics for technical advice and instrument characterization testing. Our team works closely with other institutions with extensive experience in bioaerosol measurement, such as the University of Florida-Gainesville, University of Colorado-Boulder, University of California- San Diego, FDA and RTI International. We are seeking to join a team that has interest in sampling airborne pathogens to investigate sources, sinks and the transmission of these harmful biological particles.

Selected Publications- see company website for more.

1. Maohua Pan, Tania S. Bonny, Julia Loeb, Xiao Jiang, John A. Lednicky, Arantzazu Eiguren-Fernandez, Susanne Hering, Z. Hugh Fan, Chang-Yu Wu (2017), "Collection of Viable Aerosolized Influenza Virus and Other Respiratory Viruses in a Student Health Care Center through Water-Based Condensation Growth," *mSphere*, DOI: 10.1128/mSphere.00251-17.
2. Pan, M., A. Eiguren-Fernandez, H. Hsieh, N. Afshar-Mohajer, S.V. Hering, J. Lednicky, Z. Hugh Fan and C.-Y. Wu. (2016) "Efficient collection of viable virus aerosol through laminar-flow, water-based condensational particle growth," *Journal of Applied Microbiology*, Volume 120, Issue 3, March 2016, Pages 805–815, DOI:10.1111/jam.13051.

The water-based condensation collection technology has been selected to participate in the upcoming 2018 DHS technology capability demonstration for the integration into future BioWatch monitoring instrumentation.

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PI Name	Institution	Team Name
Arvind Varsani	**Arizona State University**	**Viromics**

Project Overview

- The study of the origins, emergence, and spread of viral infections is a significant area of research in modern evolutionary biology. Drivers of viral emergence include habitat and climate change, and increased contact with reservoir species. Three stages of viral disease emergence leading to successful host switching can be identified: i) initial single infection of a new host with no onward transmission (spill-overs into "dead-end" hosts); ii) spill-overs that go on to cause local chains of transmission in new host populations before epidemic outbreaks; and iii) epidemic or sustained endemic host-to-host disease transmission within new host populations.
- Unravelling the interaction networks and assessing their propensity to change is a crucial component in efforts to fully understand the processes of viral emergence. We propose to 1) identify known and unknown viruses circulating amongst reservoirs as well as deployed personnel (less than 1% of viral diversity is currently known), 2) unravel viral dynamics within and between hosts, 3) identify viruses that are highly recombinant, thereby rapidly exploring sequence space, and the viruses most likely to spill-over into new hosts.

Teaming Overview and Objectives

- Varsani's research group at ASU: I am a molecular virologist works across ecosystems, from plants to animals, and from the tropics to the Antarctic with a strong focus on viral evolution and dynamics, and viral metagenomics. Over the years our research on single stranded DNA viruses has shown that
  1. We have grossly underestimated their diversity in ecosystems
  2. They are evolving rapidly through genetic drift (~1×10^{-3} - 8×10^{-5} sub/site/year) and are rapidly exploring sequence space through recombination and reassortment (multi-component viruses)
  3. Recombination hot-spots are located in non-coding regions of the genomes
  4. Secondary structure of DNA is important and there is strong evidence of purifying selection in paired-nucleotide sites
  5. Through recombination, they can emerge as major pathogens, e.g. maize streak virus in Africa which emerged as a serious pathogen ~250 years after the introduction of maize to the African continent
  6. Viral movements are poorly understood, in some case humans have played a role in introducing viruses into new ecosystems, in others expanded insect vector range coupled with human movement of infected material has facilitated viral epidemics
- We have fully equipped BSL2 laboratories for viral metagenomics sample processing and an infrastructure for bioinformatics analyses.
- We are looking for partners who have access to longitudinal samples from common reservoir / vector species (e.g. rats, bats, ticks, mosquitoes) so as to collect large datasets of viral sequences. We think this is essential for Phase I, especially given the fact that we know about less than 1% of viruses that exists on the planet.

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Barbara A. Han, Ph.D. Cary Institute of Ecosystem Studies

Project Overview

- **Key Expertise: Predictive analytics using machine learning**. Our team generates predictions of which species/strains are the most likely to cause spillover infection in humans using machine learning and data mining technology. Diverse data streams describing intrinsic organismal features are combined to predict hosts, vectors, pathogens with the greatest zoonotic potential.
    - Examples of past predictions we made that were subsequently confirmed by independent research groups include: mammal reservoirs of zoonotic diseases (e.g., rodents, since confirmed for 2 species in North America); filoviruses (global bats; a new bat host and new filovirus confirmed in China); mosquito vectors of flaviviruses (Zika virus subsequently isolated from a top predicted vector species in China)
    - New, unpublished predictions: primates capable of sustaining sylvatic cycle of Zika virus (Americas); zoonotic viruses with greatest potential for human-to-human transmission (global); undiscovered zoonotic tick vectors (global)
- **Contributions to PREEMPT objectives**: Our team generates data-driven predictions of organisms involved in the sylvatic transmission cycle (ie, target species from which viral jumps are the most likely); machine learning methods are applied to existing organismal data, and can be readily augmented and updated with new data (reported/collected)

Teaming Overview and Objectives

- **Team/Partners**: Members of the Han Lab (CIES), Drake Lab and members of UGA Center for Ecology of Infectious Diseases. Partners also include members of the IBM Watson Research Lab (Artificial Intelligence and Data Science teams)
- **Relevant experience**: Members have pioneered and published several papers showcasing: i) novel application of machine learning for organismal predictions, ii) novel machine learning approaches for bespoke ecological analyses; iii) novel data science methods to address technical challenges (missing data, sampling bias)
- **Team/Institutional assets**: long history of productive collaboration; data availability for several important groups (mammals, mosquitoes, Ixodes ticks); IBM Watson technology

Contact Information

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Brandon Thorpe, Ph.D.

CENTER FOR OPEN SCIENCE

Project Overview

Rigorous, reproducible research is key to both fundamental and applied research. We are a non-profit organization dedicated to providing researchers with the tools and guidance necessary to ensure a rigorous workflow, including an open-source data management, sharing and archiving platform (OSF), preregistration of study designs and analysis plans (why preregister?), and coordination of Registered Reports. Our methodological and statistical consultants ensure all results are fully reproducible and provide continual training and support for the many capabilities of OSF and scientific best practices in general.

OSF is a free-to-use central hub for collaborating across multiple teams allowing near-real-time data sharing, preservation, and version control of data, code, and all other materials. Simply plug in your favorite tools (e.g. GitHub, figshare, S3, etc.) for single sign-on access to your entire workflow, select who has access, and get to work! We can fully integrate your new tools with OSF for seamless analysis, or you can simply communicate using our public API. OSF is backed by a 50-year preservation fund so all data, code, and other materials will be available long after the program ends. See a more detailed overview of OSF capabilities and integrations here.

Preregistration clearly delineates exploratory from confirmatory research, which significantly adds to the credibility of the results. Registered Reports take this strategy further by adding peer review prior to the running experiment, plus a guarantee of publication from the journal, independent of the nature of the results. The overall impact of these strategies multiplies when a project requires many iterations of theoretical and empirical experiments. An article in Nature Human Behaviour outlines the specific problems we aim to address through preregistered analyses and the other best practices we promote.

Teaming Overview and Objectives

We are currently supporting multiple government programs, most notably the DARPA/DSO Next Generation Social Science (NGS2) program. We are serving as the Testing and Evaluation team primarily to assist performers with the technical challenges of achieving rigorous, reproducible research as detailed above. Our team consists of experienced project managers, consultants, scientists and software developers from a wide variety of backgrounds. We have a constantly growing list of partnerships and leverage our relationships with many of the top journals to ensure maximum global impact of your research.

We also have extensive experience in managing and supporting complex and rigorous research projects in addition to government programs, with a special focus on addressing the reproducibility and replicability of studies under a variety of contexts, and for multiple disciplines. *We would love to discuss how we can support your research workflow to add reproducibility and credibility to your program.*

Contact Information

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Colin Parrish Cornell University

Project Overview

- In our experimental work, my laboratory and my collaborators combine a variety of approaches to give a detailed mechanistic understanding viral emergence. The three viruses we study each transferred from one host to a new host to cause an epidemic of disease in that host.
- In our more theoretical or higher-scale studies we work with others to create models for the processes of viral emergence in new hosts, including viral spillovers, evolution of host adaptations, and the role of population form and structure in outbreak initiation.
- We would pursue the PREEMPT Technical objectives and challenges by examining models of viral epidemic emergence. Here we would use our specific and general knowledge of viral host shifting to identify and validate specific signatures of viral fitness, including general properties as well as specific mechanisms, and the potential for spillover from one species to another. We would also examine the properties of the new host populations that favor or interfere with viral emergence during the early stages of an outbreak.

Teaming Overview and Objectives

- The current collaborating team includes Colin Parrish at Cornell University, Edward Holmes at the University of Sydney, Susan Hafenstein at Penn State University, Benjamin Dalziel at Oregon State University.
- Between us we have many years of work on the experimental and modeling aspects of viral host range and emergence, as well as the molecular bases for those events, including some comprehensive reviews of the factors and the issues involved.
- We have the broad range of laboratories at Cornell, as well as other specialized facilities in structural biology and evolutionary biology.

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Prasad Paradkar CSIRO Health & Biosecurity Zoonotic Pathogens

Project Overview

The Australian Animal Health Laboratory (AAHL) is Australia's national quarantine animal health laboratory and one of the world's premier BSL4 containment facilities. This facility is unique in the South East Asia & Pacific region and provides expertise internationally to deal with global and regional biosecurity to improve preparedness against pandemic and bioterrorist threats posed by emerging infectious diseases. AAHL's microbiologically secure Large Animal Facility (LAF) is one of the world's largest and most sophisticated biocontainment research facilities, including 28 rooms in total. Two animal rooms are equipped for research at the highest level of biocontainment – BSL4. The large room measures approximately 17 meters by 6 meters. In addition to the LAF, AAHL has a separate PC4 facility that contains two BSL4 animal rooms specifically designed for work with small rodents. The LAF animal rooms can be configured to provide different types of animal accommodation, allowing us to work with a wide range of species. The insectary, located inside containment, can house a number of mosquito (and other insect) species, enabling transmission studies to relevant animal models. Our staff members have many years of experience working at BSL4 with species such as mice, guinea pigs, rabbits, ferrets, pigs, cats, dogs, bats, horses, mosquitoes and fish. The animal accommodation is also arranged to allow staff to work closely and safely with a wide variety of animal species, while minimizing any impact on the animal's freedom to express their natural behavior. We also use the latest technology in remote monitoring – including video surveillance, and body temperature sensing devices.

Given our proximity to South East Asia, expertise in working with emerging viruses, capabilities to perform biosurveillance, high throughput sequencing as well as evolution studies and perform relevant reservoir animal infection models, makes us unique in understanding natural bottlenecks involved in virus jump from reservoir species. This will enable us to determine suitable intervention strategies, which may include vaccination or genome editing of mosquitoes to break infection cycle.

Teaming Overview and Objectives

- The current team encompasses expertise in biosurveillance (mosquitoes, bats, rodents) in Australia and South East Asia, viral metagenomics, high-throughput molecular assays, viral evolution, reservoir animal models (including bats & rodents) as well as entomology and mosquito-borne viruses. Capabilities also exist in multiscale ecological and epidemiological modeling, which can be applied in this context.
- The team has published number of high-profile publications in their respective research fields.
- The team currently has on-going collaborations and projects with groups in South East Asia, which will enable access to field stations. Being a quarantine facility, relevant import permits are already in place to acquire field samples from overseas. The team also has an on-going collaboration with Omar Akbari (UCSD) for generation of genome-engineered mosquitoes.
- The main technical challenge to overcome will be pinpointing natural evolutionary bottlenecks to exploit for preventing transmission. This will be overcome by using appropriate models and experimental testing of the hypothesis. We hope to seek collaboration in this area.

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Project Overview

- Using our state-of-the-art hotspots and viral-host richness predictive machine-learning models, we will target the most important hotspot for viral surveillance in key wildlife zoonotic reservoirs (bats, rodents, non-human primates)
- We will sequence viral spike proteins and host cell receptors to analyze co-evolutionary patterns and develop predictive models of which viral strains are most likely to jump host and emerge
- We will work with our unique cell lines, and humanized lab animal models to manipulate known viruses with spike proteins of novel viral strains to test our spillover models and identify key targets for intervention
- To identify the best pathway to reduce the risk of viral emergence, we will use mathematical models of inter-species viral transmission that are ecologically and evolutionarily explicit, and test the feasibility of different approaches (gene drives, wildlife vaccination, and wildlife population manipulation).
- Using captive bat and rodents, and close relatives of viral targets, we will test our model predictions in the lab
- We will scale these approaches up to wildlife populations at closely monitored caves and mesocosms
- We will demonstrate spillover blocking proof-of-concept for a select high profile target (e.g. a bat CoV) in the wild

Teaming Overview and Objectives

- Existing team members and partners (leads):
  - EcoHealth Alliance – Peter Daszak
  - University of North Carolina - Ralph Baric
  - Columbia University – Ian Lipkin
  - NIH Rocky Mountain Lab – Vincent Munster
  - Wuhan Institute of Virology China – Zhengli Shi
  - Duke University & Singapore National University – Linfa Wang
- Experience: World leaders in modeling disease emergence (Hotspots, host-viral traits, missing zoonoses, identifying number of unknown viruses/GVP – published in *Nature*, *Science*). Tens of thousands of samples from high profile wildlife collected during last two decades globally. Intensive work on key emerging viruses (Nipah, SARS-like CoVs, SADS, MERS).
- Institutional assets: Collaborative agreements in place for Infectious disease research in humans and animals in 15 countries, including China, Malaysia, Indonesia, Jordan, Liberia and Cote d'Ivoire; BSL 3 and 4 laboratories with rodent and NHP research and genetic engineering capabilities; Current DTRA contracts for 1) Understanding Rift Valley Fever in South Africa in humans, livestock and wildlife – predicting outbreaks by developing integrated climate and immunological models. 2) Western Asia Bat Network – Research Network for Coronavirus discovery in Bats in 14 countries, 3) Special Agent Surveillance in Malaysia. Contracts from NIH and USAID on emerging viruses.

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EcoHealth Alliance

Project Overview

GeoVax is developing vaccines using a recombinant vector platform, which combines the safety and broad immunogenicity of proven vaccine vectors with the immunological advantages of virus-like particles (VLPs). With our proprietary antigen design methods, we generate live vectors that express proteins that spontaneously assemble into VLPs in the cells of the recipient. Figure 1 illustrates the assembly of VLPs in cultured cells infected with GeoVax vaccines. Our Modified Vaccinia Ankara - VLP (MVA-VLP) platform has been validated against agents including Ebola[1], Lassa[2], and Zika[3] viruses; and MVA-VLP and DNA-VLP vaccines have completed a Phase 2a trial against HIV[4, 5, 6]. For veterinary use only, we also have a Vaccinia Virus-VLP (VV-VLP) platform. Poxviruses like MVA and VV are potent and versatile vaccine vectors ideally suited for use against wildlife pathogens.

To address the PREEMPT Technical Objectives, we propose the use of MVA-VLP and VV-VLP platforms in bait vaccinations against emerging zoonotic viral pathogens. Specifically, we propose to integrate our vaccine design platform with other, complementary technologies in the areas of detection, surveillance, data analysis, manufacturing and distribution. In combination with these other technologies, our MVA-VLP and VV-VLP vaccine platforms hold great promise to provide a solution that will detect and prevent future outbreaks of zoonotic diseases.

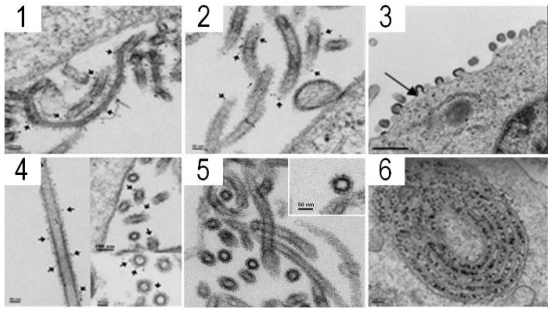

Figure 1. Electron Micrographs of VLPs Assembled from Expressed Proteins. Arrows in 1-4, specific immunogold staining. 1, EBOV; 2, SUDV; 3, HIV; 4, MARV; 5, LASV; 6, ZIKV

Teaming Overview and Objectives

VV vaccine technology is in widespread use against rabies in wildlife[7]. MVA is a VV that was attenuated in cell culture and used as a "safer smallpox vaccine" in vaccination campaigns to eradicate smallpox in the 1960s[8]. It is now widely used as a recombinant vaccine vector[9]. It has not yet been tested in bait vaccination, but it has excellent immunogenicity, and its attenuation lowers its risk profile relative to VV, particularly in terms of shedding into the environment[10]. The primary challenge to be overcome is the large-scale production of a vaccine that is orally active, highly immunogenic, and adequately safe. We believe the MVA-VLP platform will address this challenge, but we will develop VV-VLP vaccines in parallel to provide a backup strategy.

GeoVax will integrate our MVA-VLP and VV-VLP technologies with other, complementary technologies in a partnership to address the PREEMPT objectives. We have a strong history of collaboration with institutions including NIH and Duke (HIV), CDC (Zika), IHV and Scripps (Lassa vaccine), USNRL (Lassa biosensor program), Burnet (malaria), Georgia State University (Hepatitis B), and Vaxeal and Viamune (oncology). Collaborations are pending with two labs at USAMRIID for development of vaccines against Crimean-Congo hemorrhagic fever and Lassa fever, and with a military HIV research group for clinical trials against HIV. Extending on our record of collaboration, we will establish a team for proposals to PREEMPT.

Our principal technology contributions to the team are our "plug and play" recombinant vaccine vector systems for *in vivo* expression of antigens and presentation on VLPs, and our antigen design systems. The major advantages of our technology include rapid vaccine construction and screening with high confidence in success, established regulatory acceptance of vector and cell lines, proven safety of vectors, and the ability to produce large quantities of vaccines reliably and economically. We have full laboratory, quality, regulatory, and management capabilities.

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Gryphon Scientific Science. Security. Strategy.

Scientific Expertise and Analytics for Human and Animal Health

- Small business
- Rigorous applied physical and life sciences expertise
- Data and modeling decision support services
- Preparedness and response planning

GRYPHON SCIENTIFIC

Company Overview

Gryphon Scientific is staffed with SMEs with experience in epidemiological modeling, zoonotic pathogens, and vector-borne disease biology.

We provide skilled public health-related risk assessments and analyses, and expertise in scientific communications.

We can successfully support both TA1 and TA2 of the PREEMPT program, including modeling of emergence and analyses of preemptive/intervention strategies.

Gryphon has access to several datasets and tools previously developed or currently in development that are relevant to the PREEMPT program.

- Database of commercial animal populations at the county level developed for DTRA's BSVE. Includes farm and inventory counts for cattle, hogs, chickens, goats, and sheep, as well as 22 minor agricultural animal species. Includes data on regional biosafety practices.
- Regional multi-species models of the human and animal impacts and response/mitigation measures of the release of zoonotic viruses on Midwestern agricultural systems. In support of the National Bio and Agrodefense Facility risk assessment.
- Database of tick-borne disease characteristics and incidence in humans, animals, and ticks in selected US regions. Including symptomologic, epidemiologic, and ecologic characteristics.
- Model of mosquito-borne disease spread in Central and South America. Including vector and risk factor maps, and symptomologic and epidemiologic characteristics for differential diagnosis and disease burden estimation.
- Disease outbreak risk assessment tool developed for DTRA's BSVE. Assesses risk of disease spread to US from an outbreak abroad based on disease and location risk factors.
- Emerging infectious disease outbreak assessment tool developed for use by an international team of public health officials. Includes assessment of effects of intervention strategies on risk.

Teaming Overview

Gryphon Scientific is a small research and consulting firm based in Takoma Park, MD. Over 50% of our staff hold advanced degrees (MS, PhD) in scientific fields ranging from microbiology to health physics. Major clients include HHS (including NIH, CDC); DHS; and DoD (including DTRA).

- GSA Schedules 84 and 00CORP

Contact Information

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Monica Borucki LLNL Team Name

Project Overview

- Describe clearly (no jargon) what you or your team is trying to achieve using

  We aim to create a multiscale, molecular model-driven approach to predict CST using deep–sequencing to define circulating variant genotypes and protein structure models with MD simulations to identify mutations likely to impact CST. Model will estimate the number and type of mutations needed to expand virus' host range.

- Indicate how you will pursue the PREEMPT Technical objectives and the technical challenges that must be overcome.

  Technical challenges include development of predictive high-throughput screening assays and availability of crystal structures for defining protein-protein interactions. Reverse genetics and high accuracy homology models of receptor-ligand interactions will be employed to address these challenges. We would like to collaborate with DoD labsmand/or others for assembly of a multiscale analysis pipeline in regions of probable viral emergence, and for integration of molecular information into intervention strategies.

Teaming Overview and Objectives

- Existing team members and partners: Bioinformatics and protein models- Jonathan Allen and Adam Zemla. Virology- Monica Borucki

- Relevant experience (special expertise, major accomplishments, publications, etc.)

  LNL has capabilities to address: Analysis of deep sequencing data using error modeling, protein structure modeling and molecular dynamics models, molecular virology, animal models. Multiple publications describing the use of computational models to identify mutations associate with host jumps for medically significant viral families (coronavirus, paramyxovirus, rhabdovirus) and viral evolution.
- Institutional assets (specialized facilities, agreements in place, relevant collaborations with DoD labs, etc.)

  High performance computing to allow extensive macromolecular docking and MD simulations; BSL-3 facility

- Describe the technical challenges that you or your team plan to address yourselves and the additional challenges for which you are seeking collaborators.

  We will use computational modeling to address molecular scale virus-host interactions. We would like to team with others to develop high throughput bioassay development needed for testing computational predictions, and with others engaged in biosurveillance projects to enable analysis of circulating zoonotic viral genotypes.

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Metabiota, Inc

Project Overview

- Leverage existing expertise and distributed surveillance infrastructure to implement ecological viral surveillance in regions at high risk for emergence events.
- Apply multi-scale, probabilistic suitability and transmission models to surveillance, host, environmental, and viral data to quantify the risk of viral emergence and identify contributing factors.

Teaming Overview and Objectives

- Team with deep infectious disease modeling and surveillance expertise.
    - 21 MD, DVM, and PhD scientists
    - >250 year of infectious disease experience
- Implementing partner for USAID PREDICT, conducting zoonotic field surveillance in 10 African and Asian countries identified as high risk for disease emergence.
    - Collected more than 2,500 human and nearly 20,000 animal samples, performed 120,000 diagnostic tests, built capacity for diagnostic testing in 12 labs, and discovered over 150 novel viruses in genera or families known to cause human disease.
- DTRA CBEP partner with operational experience focused on biosurveillance and biosafety/security in 14 countries across four Geographic Combatant Commands.
    - "[Metabiota]'s responsiveness to emergent requirements and their ability to identify the appropriate types of technical expertise to fulfill requirements was exemplary." – CPARS official comments
- Developed epidemic analytics for NGA, DIA, and In-Q-Tel.
- Specialized expertise in infectious disease suitability mapping, phylodynamic analysis, ecological surveillance, risk analysis, software development, data management, behavioral health interventions, and capacity building.
- Opportunities for collaboration in high throughput screening methods, evolutionary modeling, and preemptive intervention evaluation.
- Technical challenges include design and implementation of sampling methodology to support QS analysis and intervention evaluation.

Contact Information

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Project Overview

- Characterize and quantify the probabilities of a viral disease emerging directly or indirectly from specific rodent reservoirs in specific areas: A multiscale model will combine information from the **micro** scale-(network model based on landscape, reservoir traits, and the genetic signatures from both rodents and viruses) with a macro-scale (spatial model) to identify the geographic areas, habitat type, and rodent species with higher probabilities for an eminent spillover event to specific human and domestic animal populations. This model will be built upon a mapping infrastructure that will become available to the community at local, regional, and global levels in a web observatory. The model will be able to be customized (adding/removing predefined variables) to achieve specific PREEMPT objectives (data release, replication, improved surveillance).
- Our model will be calibrated using landscape, genetic, and ecological data already available.
- **Team plan- Phase I**: Identify environmental conditions where viruses co-occur in rodent populations (mapping); **Phase II**: Reconstruct rodent-virus transmission rates using network models (Phase 1); **Phase III**: Forecast the propensity of virus spillover among rodent species and geographic areas; **Phase IV**: Validate model predictions in specific rodent species, and localities predicted by the model. **Project extension-optimal:** Use field data of domestic mammal species (collected in Phase 4) to add the wild-domestic interface to the spillover model.

Teaming Overview and Objectives

- Project members Dr. Gustavo Machado (North Carolina State University) and Dr. Luis E. Escobar (Virginia Tech), have a very close collaboration in animal disease ecology. Collaborating with Dr. A. Townsend Peterson (University of Kansas), and Dr. Huijie Qiao (Chinese Academy of Sciences) we have a complete team that successfully developed and implemented early warning surveillance systems.
- Team members have experience in early disease detection. The team have deep knowledge on conceptual bases, protocols, algorithms, and software for ecological modeling for detailed spillover characterization. Our expertise includes Bayesian and frequentist statistics, advanced computer analysis, remote sensing, biogeography, and infectious disease research. This experience is summarized in ~300 manuscripts developed by the team members related to animal and human infectious disease and modeling. Team member have been employed by WHO to model epidemics.
- Our project will require an extensive data-mining to identify and update virus and rodent ecological data. The number of viruses will be restricted to those of zoonotic ecology limited by the data available. We will build both micro and macro models and will be happy to collaborate with experts in phylogeography of viruses or other researchers interested in our project.

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Project Overview

- PARC developed a unique spray technology for large area and high throughput aerosol delivery of highly viscous and concentrated fluids. These fluids can include a range of solutions, e.g., bioactive formulations. This technology has a potential application in large area inoculation of animals/humans with bioengineered formulations for pre-emptive reduction of disease transfer.
- PARC has expertise in fluid/aerosol delivery, leveraging the unique spray method that can aerosolize fluids independent of viscosity or bioactive concentration. This technique enables partners in the biological space to deliver bioactive formulations to animal models with improved chance of efficacy/bioavailability. Potential technical challenges to overcome will be systems integration with rapid development/preparation of pre-emptive agents (potentially with on-demand concentration and composition) and in testing the biological response with animal models.
- PARC can have significant involvement in Technical Area 2 of a PRE-EMPT project: development of a scalable aerosol delivery method for wide-scale inoculation of animal models.

Teaming Overview and Objectives

- PARC has worked with both commercial and university partners for applications of this technology.
- PARC has expertise in fluid delivery, droplet generation, and device and systems integration drawing on our long history with developing printing systems (ink-on-paper). PARC will leverage both previous and on-going work and our related IP portfolio on fluid delivery using platform technologies (spray, transdermal delivery) to meet the PRE-EMPT program objectives.
- PARC has the institutional assets to develop and fabricate new systems for spraying, as well as the background to help improve spray formulation for uptake in mucosal and other targeted membranes.
- PARC is well-positioned to advance its unique spray technology for the PRE-EMPT program, given its demonstrated scalability and wide applicability across different fluids (ranging from low to very high viscosity and independent of bioactive concentration/loading). PARC is looking for collaborators who will investigate disease transmission across animal species and develop the necessary pre-emptive biologicals to prevent such transmission. These engineered biologicals can then be delivered to animal models using the spray technology with maximum chance for efficacy and bioavailability.

Contact Information

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Ravi Verma Spectral Platforms Looking to partner

Project Overview

Hypothesis: Zoonosis is affected by immune system and/or microbiota in the reservoir/vector/host; which in turn is affected by changing dietary patterns. Thus, the development of a working model requires tools that can characterize the linkages between (a) the changing dietary patterns and the microbiota (b) the microbiota and various aspects of the immune system, including the mucosal barrier and the inflammation state & (c) likelihood of zoonotic transmission with immune suppression.

Spectral Platforms Tools: We have developed a rapid test that can characterize the presence/absence of any pathogenic microorganism, and which can further phenotype that microorganism (at < 10 CFU/mL concentration). A preIDE meeting request for this tool has been submitted to the FDA, and we are currently negotiating a deal with an established strategic partner for commercialization. The tool is based on an engineered albumin solution that responds to very small concentrations of free radicals and enzymes produced by bacteria. The tool can be used to characterize the immune system of the reservoir/host.

Spectral Platforms Capabilities: We are also skilled in the discovery of new biomarkers. The test described above was "discovered" from a high throughput screening of various possible methods of characterizing bacterial infections. We understand that the "discovery" of the biomarker is the easy part ~ and that the real challenge involves understanding the discovery so that it can be exploited.

TA1: Develop and validate integrated, multiscale models We can characterize the immune response of the host/reservoir with our existing tools. We can also screen for new biomarkers that could characterize the (for instance) mucosal membrane. These elements could be a critical part of any good zoonosis model.

TA2: Develop scalable approaches that suppress the animal virus in its reservoir/vector Reducing the possibility of zoonotic outbreaks will require altering the dietary inputs so as to alter the immune system in either the host, or in the vector/reservoir. This will also require characterization tools that can accurately characterize the immune system in response to the changing dietary input.

Teaming We are not looking to "lead" a proposal, but are looking to join a team where our capabilities would complement. Relevant experience: We have a unique ability to characterize oxidative stress and infection status. Ours is the only rapid tool where results correlate both with blood culture positive/negative and with the time to positivity. It is the only rapid tool that can phenotype and characterize the antimicrobial susceptibility at low concentrations. Patents are pending, preIDE (for hospital use) submitted to FDA in Jan 2018. Publications expected in March 2018. Technical challenges: We are seeking a team that can has the capability to measure viral loads, and to model the zoonosis transmission. We are able to provide the tools, and also do the measurements that characterizes infection status and/or oxidative stress.

Contact Information

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PI Name: Guy Vernet Institution: the Merieux Foundation USA

Project Overview

The *Fondation Mérieux* (France) and the Merieux Foundation USA are non-profit capacity-building organizations that conduct infectious disease research in low- and middle-income countries, with the aim of increasing access to laboratory-based services and diagnostics. As part of a consortium to address technical objectives of PREEMPT, the Merieux Foundations can:

- Provide logistics, infrastructure, and personnel for field work in geographic hotspots, including support for collection of human clinical samples and animal samples
- Conduct multiplexed pathogen-specific molecular testing of field samples in BSL-2+ and BSL-3 containment within the host countries of sampling
- Conduct virus culture and deep-sequencing in its own and partner laboratories in Lyon and Beijing, and maintain quality-assured repositories of samples and isolates
- Contribute to the experimental validation of model predictions
- Contribute to the experimental validation of deployable and scalable methods to preempt viral jump across species, and analysis of long-term safety and efficacy of interventions

Teaming Overview and Objectives

The Fondation Mérieux (FMx) is headquartered in France, China and the USA, and has bureaus in Senegal, Madagascar, Lebanon and Laos. It maintains its own laboratory in Lyon, France as part of an INSERM Institute for Infectious Diseases (CIRI) that also operates one of the largest BSL-4 laboratories in europe. FMx coordinates an international research network called GABRIEL that is present in 16 countries with 20 members in LMICs, emerging and developed countries. It supports eight research laboratories (Rodolphe Merieux Laboratories) in Mali, Madagascar, Laos, Cambodia, Bangladesh, Lebanon, Brazil and Haiti, each equipped with molecular testing capacities, BSL-2+ and BSL-3 capacities and all belonging to national entities. FMx partners with the Chinese Academy of Medical Sciences and supports a research laboratory in Beijing. Expertise within FMx and the partnering laboratories comprises the diagnosis and surveillance of viral and bacterial diseases using immunoassays and molecular tools, and a strong track record of publications on the epidemiology and/or pathobiology of viruses including CCHF, influenza virus, Chikungunya virus, Zika virus, and SARS. Each of the Rodolphe Merieux laboratories constructed by FMx have been integrated within Ministries of Health, and are embedded within local universities and/or non-governmental host organisations such that they have appropriate levels of in-country government approval and authorization to conduct research. Some of them (Laos and Cambodia) also have a past history of collaboration with NAMRU-2. At the moment, staff and ongoing projects of FMx staff do not employ modelling approaches or computational biology, and thus these skills would need to provided through a consortium. Our strength and contribution to pre-empt would entail delivery of laboratory and research services within host countries, based on years of experience and using established networks of trusted partners.

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https://www.fondation-merieux.org/ and http://www.fondation-merieuxusa.org/

Luke Alphey The Pirbright Institute Team Name

Project Overview

Aims: Our aims are (TA1) to develop a robust mathematical framework for virus spread and emergence and (TA2) enhanced ability to detect and inhibit virus in mosquitoes as early-warning and prevention/mitigation tools for novel virus emergence.

Dynamic Biosurveillance (TA1): we will develop mathematical models and frameworks to scale from cellular to mosquito to epidemiology to quantify virus spread and fitness. This framework risk likelihoods and profiles for emergence of novel flavivirus strains.

Vector modification (TA2): we will develop novel genetic elements which will detect the presence of specified virus groups in mosquito vectors and reduce the ability of mosquitoes carrying these elements to transmit such viruses.

We do not know what the next emerging virus(es) will be, but at least for mosquito-borne viruses a small number of virus groups provide the overwhelming majority of human-affecting arboviruses (flaviviruses, alphaviruses and bunyaviruses), so it reasonable to assume the next emerging virus will be one of these. Of these, the flaviviruses are the most important in overall disease burden (dengue, yellow fever) and provide a recent example of a new epidemic (Zika). We will therefore focus on flaviviruses, though the approach is transferable. Development of the necessary genetic elements and engineered mosquitoes carries high technical risk of failure, which we will mitigate by pursuing multiple parallel paths and a pre-established expert sub-team for this component.

Success will provide (1) a novel mathematical framework for biosurveillance of flaviviruses and (2) a biological sensor to detect emerging viruses and, more significantly, a way to counter them. The target genetic system would provide the equivalent of having a broad-spectrum anti-viral drug or vaccine ready to deploy in the event of a new arbovirus emerging.

Teaming Overview and Objectives

Current team comprises Luke Alphey (Pirbright Institute, UK, mosquito synthetic biology including unique experience of field use of GM mosquitoes), Rennos Fragkoudis (Univ of Nottingham, UK, virologist), Andres Merits (Univ of Tartu, Estonia, molecular virologist) and Michael Bonsall (University of Oxford, UK, mathematical modelling) – the minimum skill set required to meet the aims above. Our institutes comprise all the necessary facilities, including high containment facilities at Pirbright suitable for virus challenge experiments with engineered mosquitoes. Other GM mosquito research in the Alphey lab is funded by DARPA's Safe Genes program through a subcontract from MIT.

We cover major elements of the BAA but with gaps, especially high-throughput virus screening, metagenomics and ecological surveillance. We are therefore seeking partners who can provide these and other complementary aspects. We do not need to be lead applicants.

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Omar Akbari University of California San Diego Genetic Vector Control

Project Overview

- We aim to develop new, scalable, genetic based approaches to prevent pathogen spillover and transmission from animals and vectors into humans. Our laboratory specializes in vector control for zoonotic diseases, such as Zika, chikungunya and dengue, but our technologies are easily transferable to other vector species and thus could be used to control newly emerged zoonotic vector-borne diseases.
- Our proposed goals are to utilize genetic control methods to prevent enzootic/epizootic vectors, bridge vectors or human vectors from transmitting pathogens in their sylvatic and urban cycles. These versatile and scalable methods can be utilized to rapidly replace a vector population with one refractory to infection and/or disease transmission or can reduce the vector population below the epidemic threshold. These proactive interventions essentially disarm the virus in the disease vector before it can be transmitted to the host (i.e. make a jump across species). Importantly, these methods are scalable (in the insect vector) and therefore can be readily deployed even in remote locations. Challenges of this approach will be the creation of genetic lines of the target species; however, this is our core competency and we have successfully created genetic lines for a number of mosquito species .
- Phase I: Develop and evaluate novel genetic zoonotic vector control technologies/ Phase II: Field trials

Teaming Overview and Objectives

- We are actively looking to join a team of epidemiologists and virologists that specialize in zoonotic disease modelling and disease surveillance to quantify the imminent emergence and reemergence of human pathogens. We are looking for a group that specializes Zika, chikungunya or dengue, but we are interested in discussions about our potential role in the control of any newly emerged vector-borne zoonotic disease.
- **Relevant experience:** My laboratory is currently employing genetic strategies to control disease vectors and agricultural insect pests. To date we have created the early technologies needed for genetic population suppression and replacement strategies, including multiple endogenous Cas9 expressing *Aedes aegypti* lines (Li et al. 2017, PNAS), Zika virus refractory *A. aegypti* lines (unpublished, in review) and CRISPR/Cas9 transgenesis tools for multiple anopheline malaria vectors (Li et al. 2017, G3). We are also developing novel gene drive, genetic sexing and sterile insect techniques for the control of multiples disease vectors. Furthermore, we are active in the gene drive and genetic control safety and regulation discussions and in discussions about innovating these approaches for use in non-model organisms (Akbari et al. 2015, Science; Champer et al. 2016, Nature Rev. Genetics; Adelman et al. 2017, Nature Biotech.).
- **Institutional assets:**
  The Tata Institute for Genetics and Society is a new institute has a major focus on genetic drive systems for disease vector control with sister institute in India (http://tigs.ucsd.edu/). We have also have ACL-2 insectaries and access to biosafety level 2 and 3 facilities.
- We plan to address the use of genetic vector control to prevent zoonotic disease transmission. We are seeking team members with a focus in epidemiology, virology and disease modelling to inform the best vector target(s), release thresholds and timing for this approach.

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Project Overview

Project Goal is **the development of personal virus sensor system and networking.**

The first step of preventing emerging pathogenic threats (PREEMPT) is the detection of pathogens in the fields where the pathogen source is located like animal farms and the sites for migratory birds. Although advancement of diagnostics, the pathogen detection is still limited to laboratory analysis not in real-time and not in real-fields. The team is developing a biological-treat alarm system by detecting pathogens in real-time and in real-field. **Technical Challenges** for personal virus sensor system: Total process time from sampling to detection should be short enough to be real-time. The sensor system should be portable. The sensitivity and selectivity should be comparable with the traditional laboratory sensors.

Team PVS1000 Approach: 1) *Pathogen sampling*: recently, team demonstrated a personal sampler not only collecting but also concentrating airborne nano PM (virus) and bacteria. The concentrating sample will be further enhanced during project. 2) *Real-time diagnostic*: For real-time detection, the single process from sampling to diagnostic is necessary to reduce process time. The proposing system will deliver the sample continuously without sample-preparation stops. 3) *Sensitivity & Selectivity*: the collected sample is highly concentrated. Team's sampler is thickening the concentration of pathogen in real time. The exceptional capability of thickening concentration makes the traditional diagnostic-methods available for detecting pathogens with high sensitivity and high selectivity.

Teaming Overview and Objectives

- SangYoung (SY) Son, Phd, University of Cincinnati, PI of 3 NIH projects for development of personal nanoparticle sensors. Expertise in environmental sensors, nanofluidics
- Christin M. Grabinski, Phd, US Air Force School of Aerospace Medicine, WPAFB, leaders of Hazard Assessment and Control Engineering, Expertise in validating and field-testing new approaches for characterizing health hazards and managing risk.
- James E. Lockey, MD and MS, Enmont LLC, DoD health committee, Expertise in occupational pulmonary medicine, project management.
- Chong H. Ahn, Phd, University of Cinncinnati, Expertise in Lab-on-a-chip for immunoassay, Bio-MEMS, point-of-care testing systems.

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Scott L. Nuismer University of Idaho Transmissible Vaccine

Project Overview

Recent advances in genetic engineering have opened the door to transmissible vaccines developed by inserting one or more pathogen genes with antigenic activity into the genome of a benign but transmissible vector organism. Recent theoretical work by our team has demonstrated that transmissible vaccines are powerful tools for reducing or eliminating pathogens from animal reservoir populations. Our team now seeks to move beyond the development and analysis of qualitative models by coupling quantitative, predictive models with appropriate experimental systems. Specifically, we propose to: 1) establish proof of concept for a transmissible vaccine under controlled laboratory conditions and 2) develop mathematical and computational tools for forecasting the outcome of transmissible vaccine intervention in reservoir populations of a target EID.

Teaming Overview and Objectives

Team: Scott L. Nuismer (U. Idaho), James J. Bull (UT Austin), Chris Remien (U. Idaho)

Relevant experience: Our team has extensive expertise developing and analyzing mathematical and computational models of host-pathogen coevolution, viral evolution, and transmissible vaccines.

Key publications:

Basinski, A.J. T.J. Varrelman, M.W. Smithson, R.H. May, C.H. Remien, and S.L. Nuismer. 2018. Evaluating the promise of recombinant transmissible vaccines. Vaccine. In press.

Bull, J. J., M. W. Smithson, and S. L. Nuismer. 2018. Transmissible Viral Vaccines. Trends in Microbiology 26:6-15.

Nuismer, S. L., B. M. Althouse, R. May, J. J. Bull, S. P. Stromberg, and R. Antia. 2016. Eradicating infectious disease using weakly transmissible vaccines. Proceedings of the Royal Society B-Biological Sciences 283.

Paff, M. L., S. L. Nuismer, A. D. Ellington, I. J. Molineux, R. H. May, and J. J. Bull. 2016b. Design and engineering of a transmissible antiviral defense. Journal of Biological Engineering 10.

Institutional assets: High performance computing facility; Technical support through Center for Modeling Complex Interactions and Institute for Bioinformatics and Evolutionary Studies.

Technical challenges we will address: 1) Development and analysis of mathematical and computational models guiding the development of transmissible recombinant vector vaccines, 2) Development of a mathematical and computational framework for forecasting the outcome of interventions using well-characterized transmissible vaccines

Technical challenges for which we seek collaborators: 1) Transmissible vaccine development for target EEIDs, 2) Vaccine testing and parameter estimation under controlled laboratory conditions, 3) Estimation of key parameters from natural reservoir populations.

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Project Overview – Evolution of Arboviruses in Natural Systems – Genomics for One Health

Our project will focus on the identification of environmental, evolutionary, and gene-environment interactions that facilitate the emergence of tick-borne viral pathogens at multiple scales. We will use our previous experience in modeling vector-borne disease emergence to develop empirical, simulation, and laboratory-based models that reflect realistic environmental conditions to determine how these affect the transmission dynamics of viral tick-borne pathogens among vector and zoonotic hosts, with the ultimate outcome to reduce transmission to people.

Tick vectors transmit many of the zoonotic viral pathogens that threaten the health of military service members, and yet predictive models of the emergence of tick-borne disease have lagged far behind models of diseases transmitted by other vectors. Where tick-borne disease models have been developed, they have tended to be for bacterial diseases, such as Lyme disease. Models that incorporate an interconnected web of factors, including climate and landscape, socio-behavioral, host and vector competence, and viral infectiousness, are sorely needed for tick-borne diseases.

An important aspect of our team is our ability to deliver real-time data with indices that identify spatial and temporal risk assessments for specific viral pathogens. Further, we will Incorporate evolutionary models into the predictive framework to discover "pre-emergent" pathogens, with evolutionary host switching potential as a primary risk factor.

Teaming Overview and Objectives

Our team melds the capabilities of two primary groups with foci on genomics and vector-borne diseases. At the **Woese Institute for Genomic Biology,** the **Infection Biology for One Health** team carries out research exploring the fundamental dependence of human health on the health of agricultural, industrial, and natural ecosystems. Microbes form hidden linkages that connect these ecosystems and shape their health and disease. The team has expertise in the development of predictive models for the movement of genes, genomes, and microbes among these interconnected microbial ecosystems. The **CDC Midwestern Center of Excellence for Vector-Borne Disease** was established in 2017, and includes accomplished and enthusiastic partners from Wisconsin, Illinois, Iowa, Minnesota, and Michigan. Our group includes researchers and public health experts who work together to understand and control disease pathogens carried by ticks and mosquitoes. Our team has access to a BSL-3 insectary and deep-sequencing capacities. We will also partner with the **National Center for Supercomputing Applications** Scientific Software and Applications Division to deliver dynamic and locally specific model outcomes.

Team sub-group leaders and key partners: Marilyn O'Hara Ruiz, Tony Goldberg, Rebecca Smith, Susan Paskewitz, and Rebecca Whittaker

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PI's: Drs Montse Torremorell and Meggan Craft

Project Overview

The College of Veterinary Medicine at the University of Minnesota has a major focus on identifying endemic and novel pathogens in livestock populations and modeling spread and control. This research ranges from increasing efficiency and accuracy of identification, particularly through our Veterinary Diagnostic Laboratory, to the characterization of transmission and development of disease prevention and disease elimination strategies through groups such as our Swine Disease Eradication Center.

Farmed animals are commonly implicated in spillover of zoonoses to humans. Farmers have access to an extensive set of intervention and management strategies that can prevent, eliminate or exacerbate pathogen levels within their herds. These interventions have been historically directed at diseases of economic consequence, with less focus on public health. The effectiveness of these interventions on public health has not been systematically evaluated and modeling has not been a part of strategy development. We wish to be a part of larger efforts to use mathematical, statistical, and computational models to evaluate animal production decisions in terms of infection, particularly from other reservoirs, as well as emergence and transferal to human populations.

We have extensive data on production practices, modeling, and livestock-origin pathogens at animal-human interfaces. For instance, our within-farm influenza models indicate that swine vaccination can lead to an increased number of infectious pigs after the peak of an influenza outbreak, contributing to enhanced persistence and elevated risk for antigenic drift. These findings highlight the need for a thorough understanding of the effects of herd-level management to avoid unintended consequences. We also have expertise and involvement in management of aerosol disease transmission, animal disease infection models, and strategies that suppress transmission. We have an exceptionally engaged group of stakeholders to measure and operationalize changes in pathogens and production methods, in not only the United States, but also areas such as Southeast Asia and Central Africa through our One Health Workforce Project.

Teaming Overview and Objectives

With this work we not only wish to develop better models based on our current understanding and experience with pathogen transmission, but also wish to engage in a version of 'model-guided', or potentially, in our case, 'field-led modeling' in which modelers continually engages in multidisciplinary research with our scientists and industry/public health stakeholders. We have a broad range of personnel involved in this area that includes:

Montse Torremorrell
Meggan Craft
Marie Culhane
Carol Cardona
Randall Singer
Albert Rovira
Jeff Bender
John Deen
Details of their work and more can be found at https://experts.umn.edu/

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Louis J. Gross University of Tennessee, Knoxville NIMBioS

Project Overview:
The **National Institute for Mathematical and Biological Synthesis** (NIMBioS) was established in 2008 with support from the National Science Foundation, the US Department of Homeland Security and the US Department of Agriculture as a national center to foster research and education at the interface of mathematics and biology. A particular emphasis in conjunction with its establishment was the development of novel mathematical methods to address problems associated with animal infectious diseases and the potential for zoonotic diseases to impact human populations and food security. NIMBioS has carried out a large array of research activities in infectious disease modeling through a collection of Workshops and Working Groups, involving many of the world's leading infectious diseases modelers in conjunction with experts on the diseases being considered. NIMBioS has a well-developed protocol for building expert "dream-teams" to carry out mathematical and computational modeling for infectious diseases, and a large database of experts to involve, including many associated with the University of Tennessee. NIMBioS also maintains an in-house staff of computational and data scientists with particular expertise in connecting mathematical models to data and the simulation, visualization and analysis of models using various high performance computing platforms. We thus have tremendous experience in building appropriate communities of interdisciplinary researchers to meet the PREEMPT challenges.

Team Overview and Objectives:
NIMBioS has recruited experts and supported Working Groups of ten to fifteen individuals to develop models, connect these to data and project the implications for disease transmission and spread for many diseases including: Malaria, Rabies, Toxoplasmosis, Anthrax, *Mycobacterium avium paratuberculosis*, Leptospirosis, and Zika. These activities have led to the publication of over 100 refereed papers including many in high-impact scientific journals. As just one example, NIMBioS collaborated with the National Center for Medical Intelligence and the National Science Foundation to support the effort that led to an analysis of global mapping of 355 infectious diseases (Hay et al. 2013. Phil Trans R Soc B 368: 20120250).

Leadership in multi-scale epidemiology modeling for these activities has involved many faculty at the University of Tennessee, including Louis Gross (stochastic modeling, risk assessment, multi-modeling, agent-based modeling, spatial modeling), Suzanne Lenhart (optimal control, spatial control, spatial modeling), Nina Fefferman (human social system modeling, network analysis, risk perception), and Sergey Gavrilets (cultural modeling, evolutionary dynamics of human social systems). NIMBioS maintains in-house several computational clusters with over 200 cores each, a spatial analysis lab that allows for detailed analysis of large geographic datasets, and facilities to support groups of up to forty researchers. NIMBioS maintains an in-house IT and logistics staff to manage these resources and experts in program evaluation to assess project development and refinement.

We intend to utilize our expertise in modeling to assist the development of models for PREEMPT and we are particularly interested in partners who bring laboratory and field experience in animal viral diseases with expertise in experimental methods for viral disease transmission.

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Project Overview

- **Overall Goal:** discover mechanisms that allow zoonotic, sylvatic arthropod-borne viruses (arboviruses) to jump species boundaries and cause human disease and utilize this information to anticipate and avert arbovirus emergence
- **Research Approach:** leverage our 2 active field study sites in Sarawak, Malaysian Borneo and Manaus, Brazil to prospectively investigate the ecology of sylvatic arbovirus circulation and spillover; capitalize on the viruses and vectors collected to investigate genetic signals of virus emergence potential; utilize these ecological and evolutionary data to develop and refine model-based predictions of emergence; implement control measures guided by model outputs
- **Specific Plan:** Phase I: 1. Characterize host and vector diversity and ecology, virus diversity and contact between humans and sylvatic arbovirus cycles in the field; 2. Transfer key vectors and viruses into the lab for vector competence studies, adaptation *in vivo/in vitro*, genome analyses; 3. Utilize data from 1 and 2 as foundation for models extending from virus structure to systems ecology. Phase II: Enact rationally-designed control measures, such as genetically modified vectors and/or microbiome modifications, novel vaccine approaches and therapeutic/preventative therapy based on antibodies. In Phase II, we will also validate and integrate our developed models of risk assessment and validate emergence outcomes based on our developed intervention approaches.

Teaming Overview and Objectives

UTMB: Drs Vasilakis, Weaver, Routh, Rossi; **NMSU**: Drs Hanley, Bueneman, Althouse, UAV team

UPR: Dr. Sariol; **WUSL**: Dr. Diamond; **JHU**: Dr. Dimopoulos; **Cary Inst**: Dr. Han; **QUT (Australia)**: Drs. Aaskov, Devine; **UNIMAS (Malaysia):** Drs. Perera, Ooi; **FMT-HVD (Brazil):** Drs. Lacerda, Mourao, Chaves

Our Team has been at the forefront of Enzootic Arbovirus emergence over the past 20 years with many seminal publications on the ecology and emergence potential of Zika, Dengue and Chikungunya through field studies in Peru, Senegal, Borneo and Brazil. The team was instrumental in discovering and characterizing a new DENV serotype (DENV-5) that has not yet emerged in the human transmission cycle as well as identifying the molecular and evolutionary components of CHIKV emergence

UTMB is the only academic institution with Biosafety facilities to BSL4 including vivariums and insectaries, home to World Reference Collection of Emerging Viruses and Arboviruses, numerous centers centered on Biodefense, vaccine development, Translational Research, long term collaborative agreements with Malaysian and Brazilian partners, as well as DoD and HHS collaborations.

To gain uninterrupted access to the forest canopy for collection of enzootic arboviruses we will use a novel technology using unmanned aerial vehicles (UAVs). However, our team would require expertise in structural modeling to allow modeling of the adaptive mutations on the target protein's crystal structure to gain insights into the evolution, expansion of host range, interaction and/or targeting receptors

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